

Exhibit 4

HIGHLY CONFIDENTIAL: SUBJECT TO PROTECTIVE ORDER

**IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF OHIO EASTERN DIVISION**

IN RE NATIONAL PRESCRIPTION
OPIATE LITIGATION

County of Summit, Ohio, et al.

v.

Purdue Pharma L.P., et al.

The County of Cuyahoga

v.

Purdue Pharma L.P., et al.

CASE NO. 1:17-MD-2804

JUDGE POLSTER

TRACK ONE CASES

EXPERT REPORT OF PROFESSOR MARGARET K. KYLE

May 10, 2019

Expert Report of Margaret K. Kyle, PhD

or did not say about Norco, and thus offers no evidence that these payments were unlawful.⁸³ The U.S. Department of Health and Human Services (“HHS”) Office of the Inspector General (“OIG”) acknowledged in its April 2003 “Compliance Program Guidance for Pharmaceutical Manufacturers” that grants paid to speakers may be appropriate under certain conditions.⁸⁴ The Pharmaceutical Research and Manufacturers of America (“PhRMA”) published a “code on relationships with U.S. healthcare professionals” effective July 2002, and it updated the code effective January 2009. The PhRMA code also permits “speaker programs and speaker training meetings” under certain conditions.⁸⁵ The OIG states in its guidance that “the PhRMA Code...will substantially reduce the risk of fraud and abuse and help demonstrate a good faith effort to comply with the applicable federal health care program requirements.”⁸⁶

- (49) Allergan promoted Kadian between 2009 and 2013 by detailing physicians. After the December 30, 2008 Kadian acquisition closed, Allergan did not initially plan to detail Kadian to doctors.⁸⁷ Only after Allergan discovered that other companies were telling prescribers and wholesalers that Kadian had been discontinued did Allergan decide that it might be worthwhile “to let physicians know that [the] product was still available.”⁸⁸
- (50) The Kadian patent was set to expire in April 2010, which would invite generic entry, meaning that Kadian had a short remaining product life.⁸⁹ According to Actavis’s CEO Doug Boothe, “[w]e had no aspirations that we were going to increase the scripts. We were trying to slow down the rate in which prescriptions stopped.”⁹⁰ To that end, on May 1, 2009, Allergan hired a contract salesforce through Ventiv Commercial Services, LLC (“Ventiv”) to detail Kadian to prescribers.⁹¹ Allergan implemented a small, 18-member Kadian salesforce supervised by two managers called “regional business directors.”⁹² The salesforce’s goal was “to let prescribers know that the product was available and to

⁸³ Perri April 24 Dep. at 600:1–25; 602:17–603:16; 605:7–18; 605:23–606:12 (objections omitted).

⁸⁴ Office of Inspector General, U.S. Department of Health and Human Services, “Compliance Program Guidance for Pharmaceutical Manufacturers,” April 2003, p. 21, available at <https://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacymfgnonfr.pdf>.

⁸⁵ PhRMA, “Code on Interactions with Healthcare Professionals,” revised July 2008 and effective January 2009, pp. 3, 9–10, available at <https://www.acpe-accredit.org/pdf/Code%20on%20Interactions%20HC%20Professionals.pdf>.

⁸⁶ Office of Inspector General, U.S. Department of Health and Human Services, “Compliance Program Guidance for Pharmaceutical Manufacturers,” April 2003, p. 31, available at <https://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacymfgnonfr.pdf>.

⁸⁷ ALLERGAN_MDL_01190060 at -0060.

⁸⁸ Boothe Dep. at 175:8–176:4; Actavis “knew that Alpharma hadn’t been talking about the product for a while, the reps hadn’t been promoting Kadian” so Actavis’s “main goal was just to make prescribers aware ... that Kadian was available.” *See* Deposition of Nathalie Leitch, January 22, 2019 [hereinafter “Leitch Dep.”] at 44:20–45:14.

⁸⁹ Leitch Dep. at 37:15–38:12.

⁹⁰ Boothe Dep. at 176:5–177:8.

⁹¹ *See* Allergan’s Fourth Amended Objections and Responses to Plaintiffs’ Corrected Second Set of Interrogatories, *In re National Prescription Opiate Litigation*, MDL No. 2804, Case No. 17-md-2804 (N.D.Ohio Mar. 4, 2019.) pp. 35–38.

⁹² Boothe Dep. at 176:5–177:8, 323:10–325:11; Leitch Dep. at 40:17–41:5.

provide information about the product.”⁹³ The contract salesforce’s promotion was essentially an awareness campaign that attempted to stem the decline in Kadian prescribing.⁹⁴

(51) At the outset of detailing, Allergan used marketing materials that Alpharma had created.⁹⁵ Then, on February 18, 2010, Allergan received a warning letter regarding those materials.⁹⁶ As discussed in detail below, Allergan took prompt corrective action in response to the warning letter. As part of its response, Allergan hired a consultant named Jennifer Altier to create new marketing materials.⁹⁷ Ms. Altier testified that, after the warning letter, Allergan “took a very conservative approach”; specifically, she described the marketing materials as a “colorful [package insert (“PI”)],” and she testified that they were “really just reflective of the information that was in the PI, sticking with the label, remaining within the FDA guidelines.”⁹⁸ Professor Perri confirmed that numerous Kadian marketing materials contained statements taken directly from the FDA approval letter for Kadian and the Kadian PI.⁹⁹ Those materials also were submitted to the FDA for its review prior to use.¹⁰⁰

(52) Professor Perri also admits that Kadian marketing materials show that sales representatives “were specifically directed to discuss safety considerations with prescribers during sales calls.”¹⁰¹ In fact, Professor Perri cites a presentation given at the 2011 National Sales Meeting for Kadian.¹⁰² That presentation contains a “Do’s” and “Don’ts” section. Under the “Do’s” section, Allergan instructed the sales representatives to “discuss safety considerations associated with Kadian with prescribers during sales calls,” and to “communicate the full indication for Kadian during discussions with prescribers.”¹⁰³ Under the “Don’ts” section, Allergan instructed the sales representatives not to make comparative product claims or unsubstantiated efficacy claims: specifically, Allergan explained that there is no substantial evidence demonstrating that Kadian improves functioning or quality of life, and thus, the sales representatives were prohibited from making that kind of claim.¹⁰⁴ Numerous Kadian training presentations include similar instructions.¹⁰⁵

⁹³ Leitch Dep. at 61:5–10.

⁹⁴ Leitch Dep. at 100:1–19; *See also* Altier Dep. at 369:19–370:1; Leitch Dep. at 44:20–45:11; “Given patents for the product expire in April 2010, our strategy needed to be a greatly rationalized approach versus what Alpharma had done in the past.” *See* ALLERGAN_MDL_01692522 at 2522–2524.

⁹⁵ Leitch Dep. at 127:10–17.

⁹⁶ ALLERGAN_MDL_00795835 at -5835-5847; Altier Dep. at 83:5–14.

⁹⁷ Altier Dep. at 367:2–7.

⁹⁸ Altier Dep. at 94:22–95:9; *See also* Perri April 24 Dep. at 614:13–24.

⁹⁹ Perri Dep. at 581:10–596:4 (objections omitted).

¹⁰⁰ Boothe Dep. at 170:17–171:7.

¹⁰¹ Perri Rep. ¶ 123.

¹⁰² Perri Rep. fn 246.

¹⁰³ ACTAVIS0413281 at -3293.

¹⁰⁴ ACTAVIS0413281 at -3296.

¹⁰⁵ *See e.g.*, ALLERGAN_MDL_00405530 at -5566–5572;

ALLERGAN_MDL_01199237 at -9247–9250;

Expert Report of Margaret K. Kyle, PhD

the sales representatives were instructed to respond that they were permitted to provide information about Kadian, not to discuss other long-acting opioids¹³⁵ As Professor Perri admits, many (if not all) of the statements in the Objection Handling Workshop come directly from the FDA approval letter for Kadian or the Kadian package insert (PI).¹³⁶

(64) Allergan recognized that its “targeting focus can’t be so narrow that we miss opportunities with targets who write a little Kadian BUT large amounts of morphine (i.e. morphine sulfate, Avinza).”¹³⁷ Thus, Allergan decided to target high morphine and Avinza writers in addition to high generic morphine writers.¹³⁸ In fact, Allergan hired additional representatives called “Area Business Specialists” who were specifically “charged with targeting high volume prescribers of generic morphine sulfate who are currently prescribing little to no Kadian and turning them into Kadian prescribers. This expansion is an extension of our overall strategy to capture prescriptions that might otherwise go to the generic product.”¹³⁹

(65) In sum, I am not aware of evidence that Allergan’s promotional focus was to start patients on Kadian who would not otherwise be prescribed an opioid.

II.C.3. Kadian corrective action

(66) On February 18, 2010, the FDA issued a warning letter to Allergan claiming that two Kadian promotional materials—a “Co-Pay Assistance Program brochure”¹⁴⁰ and a “PK to PK Comparison Detailer”¹⁴¹—contained false or misleading information for allegedly (1) omitting and minimizing risk information, (2) broadening the Kadian indication and failing to state the full Kadian indication, (3) making unsubstantiated superiority claims, and (4) containing unsubstantiated effectiveness claims.¹⁴² Allergan took corrective action almost immediately after receiving the warning letter. Below I provide a timeline of events concerning Allergan’s response:

- **February 19:** Allergan forwarded the warning letter to the sales representatives instructing them to “immediately cease” disseminating these materials and to quarantine all Kadian promotional materials in the field until further notice because they too could contain messages similar to those

¹³⁵ See ALLERGAN_MDL_00405512.

¹³⁶ Perri Dep. at 581:10–596:4 (objections omitted).

¹³⁷ ALLERGAN_MDL_00402219 at 7.

¹³⁸ ALLERGAN_MDL_00402219 at 13; *See also* ALLERGAN_MDL_00397937 at 16 (noting that Actavis’s goal was to maximize Kadian sales “by converting high volume MS prescribers to Kadian.”); ACTAVIS0197924 at 34–35 (listing questions that the sales representatives to ask prescribers for purposes of obtaining switches from generic morphine and Avinza without making comparative product claims).

¹³⁹ ALLERGAN_MDL_00418998 at -8998.

¹⁴⁰ ALLERGAN_MDL_00440829.

¹⁴¹ ALLERGAN_MDL_01103851 at 3851–3852.

¹⁴² ALLERGAN_MDL_00795835 at -5835-5847.

Expert Report of Margaret K. Kyle, PhD

at issue in the warning letter. Promotion was permitted to continue, but all promotion had to be limited to the copay cards (without the brochure) and the Kadian PI.¹⁴³

- **February 21:** Ventiv forwarded Allergan's letter and the warning letter to the salesforce, instructing that the team may not use the Kadian promotional materials and explaining that all promotional materials—except the copay card itself and the Kadian PI—had to be held.¹⁴⁴
- **March 4:** Allergan responded to the FDA warning letter, informing the FDA that the sales representatives were instructed to cease using materials containing the challenged statements and to return them to Allergan for destruction. Allergan also proposed a corrective-action plan, which included proposed “Dear Healthcare Professional” and “Dear Consumer” letters to be sent to those who had received the offending promotional materials.¹⁴⁵
- **March 9:** Allergan instructed the Kadian sales representatives to return all promotional materials either in their possession or that could be obtained for destruction.¹⁴⁶
- **March 26:** FDA responded to Allergan’s March 4 letter, generally agreeing with Allergan’s corrective-action plan and requesting that Allergan send the proposed “Dear Healthcare Letter” to anyone who could have received the Comparison Detailer.¹⁴⁷
- **April 9:** Allergan responded to the FDA’s March 26 letter confirming that the “Dear Healthcare Letter” would be sent to any prescriber that could have been exposed to the Comparison Detailer. Allergan also recommended sending the “Dear Consumer” letters to patients directly or to physicians’ offices.¹⁴⁸
- **April 19:** FDA responded to Allergan’s April 9 letter, requesting that Allergan deliver 100 copies of the “Dear Consumer” letter to prescribers and that physicians have these letters for 90 days.¹⁴⁹
- **May 3:** Allergan responded to the FDA’s April 19 letter, agreeing to the FDA’s plan. Allergan also promised to call any prescribers not personally visited to see if the prescribers needed additional letters.¹⁵⁰

¹⁴³ ALLERGAN_MDL_01869494; ALLERGAN_MDL_01869495; ALLERGAN_MDL_01869507.

¹⁴⁴ ALLERGAN_MDL_01869510 at 9510–9511;

ALLERGAN_MDL_01869512;

ALLERGAN_MDL_01869524.

¹⁴⁵ ALLERGAN_MDL_01396751.

¹⁴⁶ ALLERGAN_MDL_01436179.

¹⁴⁷ ALLERGAN_MDL_01866384.

¹⁴⁸ ALLERGAN_MDL_01399387.

¹⁴⁹ ALLERGAN_MDL_01874806.

¹⁵⁰ ALLERGAN_MDL_01875958.

Expert Report of Margaret K. Kyle, PhD

- **May 20:** FDA responded to Allergan's May 3 letter, requesting that Allergan "physically visit" each prescriber to set up a stand with the "Dear Consumer" letters, and to follow up with the prescribers by calling them each month for 90 days.¹⁵¹
- **June 10:** Allergan responded to the FDA's May 20 letter, again agreeing to the FDA's proposed plan and committing to personally visit roughly 10,000 prescriber offices and over 550 pharmacies that had received copay materials from Allergan. Allergan would temporarily expand its sales team to accomplish this corrective action.¹⁵²
- **June 29:** Allergan sent TMS Health a revised telemarketing script to account for the warning letter's concerns.¹⁵³
- **July 6:** FDA responded to Allergan's June 10 letter, agreeing with Allergan's plan regarding the "Dear Doctor" letter. FDA also agreed with Allergan's intentions of mailing the "Dear Healthcare Professional" letter to those prescribers who might have received the Comparison Detailer.¹⁵⁴
- **July 7–8:** Allergan trained new sales representatives with the corrected message.¹⁵⁵ Training included presentations on the Kadian PI,¹⁵⁶ Kadian marketing materials,¹⁵⁷ objection handling,¹⁵⁸ and Kadian support programs.¹⁵⁹
- **July 16:** Allergan responded to the FDA's July 6 letter explaining that 7,163 physicians would be receiving "Dear Healthcare Professional" letters via mail.¹⁶⁰
- **August 4:** FDA responded to Allergan's July 16 letter, signing off on Allergan's plan.¹⁶¹ In addition, Allergan conducted corrective-message training for its sales representatives.¹⁶²
- **August 10:** Allergan informed Ventiv that, during the corrective-action period, the sales representatives were prohibited from making regular sales calls. Allergan further explained that it will be mailing a "Dear Healthcare Professional" letter to all healthcare professionals who potentially received the Comparison Detailer, and that the sales representatives would hand deliver copies of the "Dear Consumer" letter to prescribers and pharmacies that received the Co-

¹⁵¹ ALLERGAN_MDL_01868671.

¹⁵² ALLERGAN_MDL_01399410 at -9411.

¹⁵³ ALLERGAN_MDL_00436590.

¹⁵⁴ ALLERGAN_MDL_01869099.

¹⁵⁵ ALLERGAN_MDL_01897644.

¹⁵⁶ ALLERGAN_MDL_00405530 at -5530-5572.

¹⁵⁷ ALLERGAN_MDL_00435872.

¹⁵⁸ ALLERGAN_MDL_00405512.

¹⁵⁹ ALLERGAN_MDL_00405573.

¹⁶⁰ ALLERGAN_MDL_01237743 at -7743-7762.

¹⁶¹ ALLERGAN_MDL_01238281 at -8281-8284.

¹⁶² ALLERGAN_MDL_01051295 at 1295-1333.

Pay Assistance Program brochure. To accomplish this corrective action, Allergan would hire an additional 175 temporary sales representatives.¹⁶³

- **August 18:** Allergan finalizes the “Dear Healthcare Professional”¹⁶⁴ and “Dear Consumer”¹⁶⁵ letters for submission to the FDA.
- **August 19:** Allergan and Vantiv conducted corrective-action rollout training for the salesforce.¹⁶⁶
- **August 23:** The corrective-action campaign began. Sales representatives were prohibited from making regular sales calls during this time.¹⁶⁷
- **September 10:** Although the sales representatives had nearly completed their corrective-action campaign, they were instructed not to resume promotion until Allergan gave permission.¹⁶⁸
- **September 26:** Allergan informed the sales representatives that Kadian promotional activities were permitted to resume “only if you have completed dissemination of the corrective action materials to all of your targets.”¹⁶⁹
- **November 1:** Allergan informed the FDA that it had completed disseminating the “Dear Healthcare Professional” and “Dear Consumer” letters and that the salesforce would be conducting follow-up calls to each prescriber and pharmacy.¹⁷⁰

¹⁶³ ALLERGAN_MDL_01110478 at 0478-0480.

¹⁶⁴ ALLERGAN_MDL_01110407 at 0407-0413.

¹⁶⁵ ALLERGAN_MDL_01110403 at 0403-0406.

¹⁶⁶ ALLERGAN_MDL_00435497 at -5497-5526.

¹⁶⁷ ALLERGAN_MDL_01115903 at -5903-5910.

¹⁶⁸ ALLERGAN_MDL_01897894 at -7894.

¹⁶⁹ ALLERGAN_MDL_01419292 at -9292. (emphasis in original).

¹⁷⁰ ALLERGAN_MDL_02106570 at -6570.

Expert Report of Margaret K. Kyle, PhD

A. I really have no idea about whether such details exist. My model includes all detailing over the period from 1995 to 2018 based on the instruction that I was given to consider that unlawful.

Q. Okay. Without distinguishing between the quality or extent of those detailing visits?

A. I do not distinguish among those details, no.¹⁸¹

III.D. Allergan's prescription opioids accounted for a fraction of 1% of all prescribed opioids

(77) Kadian and Norco account for an extremely small share of opioid MMEs in Cuyahoga and Summit counties, and nationally. These small shares underscore the limited scope and magnitude of Allergan's promotion of these two products. In Figure 6–Figure 8, I list by year the share of opioid MMEs associated with Kadian and Norco in Cuyahoga and Summit counties, and nationally, respectively. I exclude shares prior to 2009 for Kadian because Alpharma owned and promoted Kadian during that time. Allergan's combined share of opioid MMEs over the time period from January 1997–April 2018 was approximately 0.27% in both Cuyahoga and Summit counties. This is slightly lower than in the rest of the nation, where Allergan's combined share was 0.40%. In Cuyahoga and Summit counties, neither Kadian nor Norco accounted for more than 1% in any year.¹⁸² These figures are consistent with the analysis of Plaintiffs' expert Dr. McCann, who calculates that Allergan shipments account for 0.00% of MMEs in Cuyahoga and Summit counties during the period 2006–2014.¹⁸³

¹⁸¹ Rosenthal May 4 Dep. at 217:20–218:14 (objections omitted).

¹⁸² I limit my share analysis to 1997–2018 because data with prescriber location are unavailable prior to 1997.

¹⁸³ Second Supplemental Report of Craig J. McCann, April 15, 2019 at Appendix 1.

Figure 6: Allergan product shares of all opioid MMEs in Cuyahoga County, by year¹⁸⁴

Year	Kadian	Norco	Total
1997		0.00%	0.00%
1998		0.19%	0.19%
1999		0.58%	0.58%
2000		0.61%	0.61%
2001		0.19%	0.19%
2002		0.19%	0.19%
2003		0.13%	0.13%
2004		0.09%	0.09%
2005		0.09%	0.09%
2006		0.06%	0.06%
2007		0.04%	0.04%
2008		0.03%	0.03%
2009	0.94%	0.02%	0.96%
2010	0.72%	0.02%	0.74%
2011	0.65%	0.01%	0.66%
2012	0.13%	0.01%	0.15%
2013	0.07%	0.03%	0.10%
2014	0.07%	0.02%	0.08%
2015	0.06%	0.01%	0.08%
2016	0.06%	0.01%	0.08%
2017	0.07%	0.01%	0.08%
1997-2017	0.20%	0.06%	0.26%

Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data.

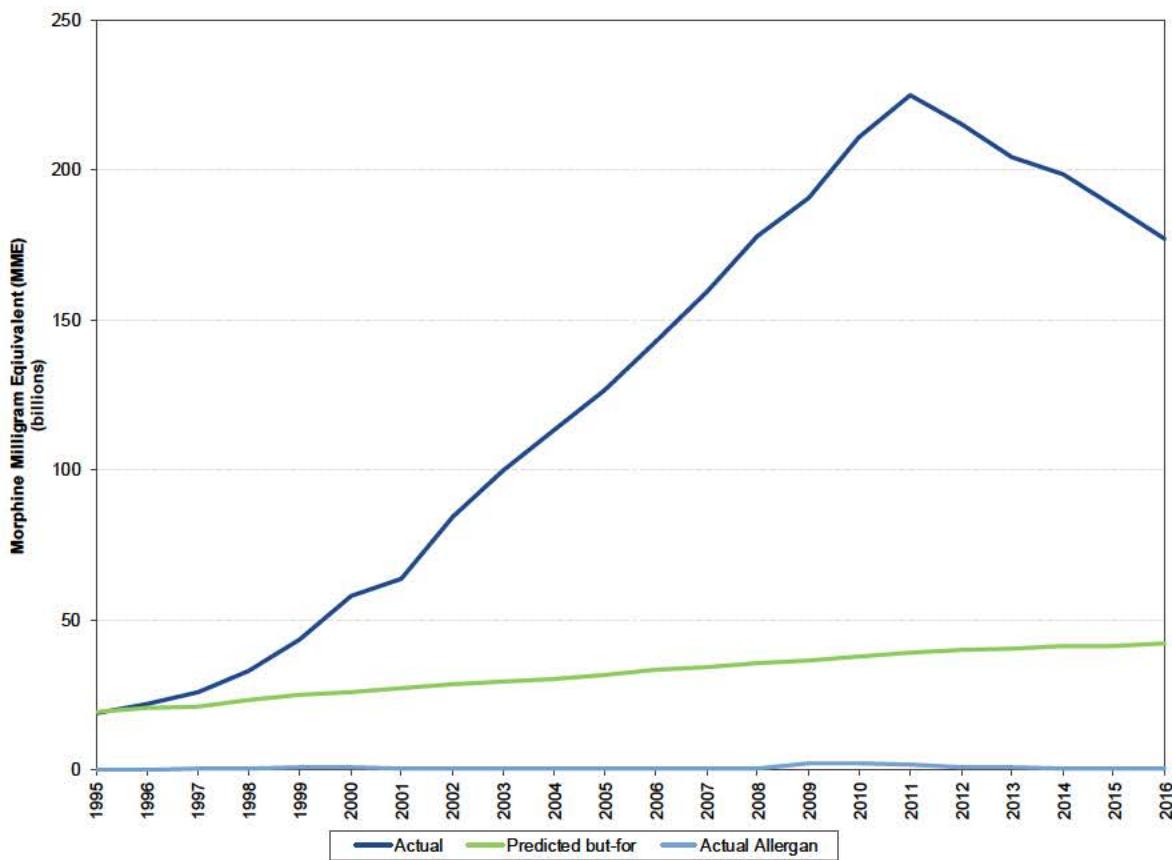
¹⁸⁴ I include in the denominator of my share calculations in Figures 6–8 the same opioid products that were analyzed by Professor Rosenthal, which I understand includes opioid products that were at any point classified as Schedule II, plus Butrans. Throughout this report, my references to “opioids” are limited accordingly unless otherwise noted. (In her report, Professor Rosenthal incorrectly describes her limitation as including only “class II *oral* opioid products plus Butrans.” However, her Appendix C tables and backup production clearly include non-oral opioids, such as Duragesic.) See Rosenthal Rep. Table C.5, C.6.

Figure 7: Allergan product shares of all opioid MMEs in Summit County, by year

Year	Kadian	Norco	Total
1997		0.00%	0.00%
1998		0.17%	0.17%
1999		0.30%	0.30%
2000		0.17%	0.17%
2001		0.17%	0.17%
2002		0.18%	0.18%
2003		0.13%	0.13%
2004		0.08%	0.08%
2005		0.08%	0.08%
2006		0.06%	0.06%
2007		0.06%	0.06%
2008		0.04%	0.04%
2009	0.77%	0.02%	0.79%
2010	0.76%	0.02%	0.78%
2011	0.76%	0.01%	0.77%
2012	0.20%	0.02%	0.21%
2013	0.14%	0.03%	0.17%
2014	0.05%	0.03%	0.08%
2015	0.02%	0.02%	0.04%
2016	0.02%	0.01%	0.04%
2017	0.02%	0.01%	0.03%
1997-2017	0.21%	0.06%	0.27%

Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data.

Figure 11: Kadian and Norco MME's in the context of Professor Rosenthal's "maximum...clinically justifiable" analysis



Source: Rosenthal backup data.

(81) Plaintiffs' models cannot credibly conclude that any portion of the alleged harms is attributed to Allergan considering Allergan's extremely small share of all opioid MMEs, particularly in the context of the unquantified uncertainty surrounding the estimates offered by Plaintiffs' economic experts. Although Plaintiffs' economic experts have neglected to quantify this uncertainty, each of their estimates have error bounds that compound when they are multiplied together by Professor McGuire to calculate damages. Even a small level of uncertainty would make it virtually impossible to discern whether Allergan's extremely small share of all opioid MMEs caused any expansion in opioid prescribing.

Expert Report of Margaret K. Kyle, PhD

IV. Plaintiffs have not shown that Allergan's promotion expanded opioid prescribing, let alone improper prescribing

(82) The causation and damages approach offered by Plaintiffs' economic experts purportedly assesses the extent to which increases in manufacturer detailing resulted in *additional* prescribing. Professor Rosenthal explained this in her deposition:

Q. Does your model account for rivalrous marketing?

...

A. The aggregate model that I put forth is intended to essentially obscure the rivalrous marketing, so to the extent that marketing only moves people from hydrocodone to oxycodone or the other direction, whatever it is, that will show up as a noneffect in my model. So I'm only looking at market expansion because the question I care about is market expansion.¹⁸⁹

As further discussed below, although Professor Rosenthal claims that rivalrous marketing would show up as a "noneffect" in her model, the reality is that she applies the average effect of detailing to every manufacturer, regardless of whether all of their marketing was rivalrous or none of it was. Because Professor Rosenthal's approach assumes that all detailing has the same incremental effect, it fails to consider whether some detailing (e.g., detailing associated with certain manufacturers, products, or types of products) had no effect on total prescribing or resulted in prescribers switching from opioids they were already prescribing. This has the effect of penalizing defendants whose marketing was primarily rivalrous. In this section, I demonstrate that Plaintiffs' experts have failed to demonstrate that Allergan's promotion expanded opioid prescribing because they have not accounted for the rivalrous nature of that promotion. I also analyze Ohio Automated Reporting Rx Reporting System ("OARRS") data, which Plaintiffs' economic experts have ignored, to demonstrate that prescriber- and patient-specific patterns of Kadian prescribing are consistent with rivalrous marketing and with providers exercising their clinical discretion. I demonstrate the following in this section:

- Professor Rosenthal's models inappropriately assume that all manufacturer promotion equally impacted opioid prescribing.
- Allergan's extremely low share and timing of opioid MMEs in Cuyahoga and Summit counties (i.e., less than 0.3% as listed in Figure 6 and Figure 7) demonstrate that Allergan's promotion did not contribute materially to an overall increase in opioid prescribing.

¹⁸⁹ Rosenthal May 4 Dep. at 206:10–206:25 (objections omitted).

Expert Report of Margaret K. Kyle, PhD

- Allergan deposition testimony and contemporaneous sales documents reflect Allergan's objective to take volume from competing products rather than to expand overall opioid prescribing.
- Provider-specific prescribing and detailing data for Kadian—data ignored by Plaintiffs' economic experts—demonstrate that prescribers Allergan detailed in Cuyahoga or Summit counties routinely did not increase their Kadian prescribing relative to the level of Kadian prescribing prior to Allergan's acquisition from Alpharma.
- Patient-level prescribing patterns for the Allergan-detailed prescribers I was able to identify in the Ohio Automated Reporting Rx Reporting System (“OARRS”) data for Cuyahoga and Summit counties reflect that they prescribed Kadian to only a small subset of their patients; that they typically prescribed only a few Kadian scripts per patient, in many instances at low MMEs per day; and that prescribers used discretion when prescribing Kadian, taking patient-specific characteristics into account.

IV.A. Professor Rosenthal assumes that the promotion of all manufacturers, including defendants and non-defendants, equally impacted opioid prescribing

(83) Professor Rosenthal's direct model makes the untested assumption that the promotion of all manufacturers (both defendant and non-defendant) and of all types (using detailing as a proxy), whether lawful or allegedly unlawful, was equally persuasive to physicians to prescribe opioids. This assumption is inconsistent with Plaintiffs' allegations regarding the allegedly deceptive practices of individual defendants described above, and the assumption is not supported by the literature on pharmaceutical promotion. For example:

- Berndt et al. (1995), cited by Professor Rosenthal, note that promotion can be industry expanding or rivalrous, and that the effect of marketing depends on market structure. Specifically, they find that order of entry effects are important, with a strong first-mover advantage. The promotional efforts of later entrants are more likely to be rivalrous, i.e., to substitute for existing products rather than to expand the market. It is therefore not appropriate to assume that all manufacturer promotion affected aggregate shipments in the same way.¹⁹⁰
- Studies of the economics of advertising, including at least one authored by Professor Rosenthal, often use the theoretical model of Dorfman and Steiner (1954), who derive the optimal advertising to sales ratio as equal to the ratio of the elasticity of sales with respect to advertising and the elasticity of sales with respect to price.¹⁹¹ In her study, firms vary considerably in the ratio

¹⁹⁰ See Ernst R. Berndt, Linda Bui et al., “Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market,” American Economic Review 85, no. 2 (1995), 100–105.

¹⁹¹ Meredith B. Rosenthal, Ernst R. Berndt, Julie M. Donohue, “Demand Effects of Recent Changes in Prescription Drug Promotion,” in *Frontiers in Health Policy Research*, Vol. 6, eds. David M. Cutler and Alan M. Garber, 1–26

of advertising to sales. This implies that firms are also likely to differ in their elasticity of sales with respect to advertising (i.e., their advertising has differential effects on sales).

- Datta and Dave (2017), also cited by Professor Rosenthal, find that detailing affected brand-specific demand but had no impact on total demand for the class of drugs studied.¹⁹² This study used a much richer dataset than that used by Professor Rosenthal, which allowed the authors to control for other factors that affect prescribing behavior, such as physician characteristics, which Professor Rosenthal ignored.

(84) Professor Rosenthal claims that her model allows for a recalculation of but-for harm if a defendant is exempted from liability because its messages were not found to be unlawful, but key assumptions—namely that all marketing regardless of type, content, or time period has the same impact on sales, and that all incremental sales are equally harmful—are still inherent in her calculations and are never tested. Rather, her sensitivities simply (1) apply the average effects from her aggregate direct model to every manufacturer regardless of the nature of its promotional activity relative to other manufacturers, and (2) scale those effects based on the manufacturer’s amount of detailing.¹⁹³ This is inappropriate if detailing’s effects changed over time or differed across manufacturers or products. For example, for the first entrants, detailing may have expanded the market, while later entrants’ efforts may have focused more on encouraging a doctor to use the specific opioid being detailed, rather than any opioid.¹⁹⁴ This is also inappropriate if the products vary in the extent to which they are substitutable. Long-acting products are closer substitutes to other long-acting products than to short-acting products, for example.¹⁹⁵ Detailing of a long-acting product is unlikely to affect prescriptions of long-acting opioids and short-acting opioids in the same way.

(85) In past litigation, Professor Rosenthal has acknowledged the importance of differentiating promotion for different products and by different manufacturers in the same class, noting that promotion of one product has a positive effect on that products’ volume and a negative effect on competitor volume. For that reason, she included separate measures for different manufacturers’ promotion in those models (which she failed to do here).

(Cambridge, MA: The MIT Press, 2003).

¹⁹² See Rosenthal Rep. ¶ 34.

¹⁹³ Compounding these issues described above, Professor Rosenthal also inappropriately attributes products to Allergan in some time periods. For example, she inappropriately assigns Anexia to Allergan. See Rosenthal Rep. Table C.6.

¹⁹⁴ See Ernst R. Berndt, Linda Bui et al., “Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market,” *American Economic Review* 85, no. 2 (1995), 100–105.

¹⁹⁵ See e.g., Federal Trade Commission, “Analysis of the Agreement Containing Consent Order to Aid Public Comment,” *In the Matter of King Pharmaceuticals, Inc. and Alpharma Inc.*, December 29, 2009; Respondent Impax Laboratories, Inc.’s Replies to Complaint Counsel’s Proposed Findings of Fact and Conclusions of Law, *In the Matter of: IMPAX LABORATORIES, INC.*, February 13, 2018; ALLERGAN_MDL_00044009 at -4009–4021; PPLPC030000994661 at sheet Past 10 Yr Pdts Launch Aligned.

The key explanatory variables include the level of spending on promotion, both for Zyprexa and for the other atypical antipsychotics with which it competes, the prices for Zyprexa and its competitors, as well as other market events including the entry date of specific competitive atypical antipsychotics and the FDA warning in late 2003...Based on economic theory and evidence reviewed above, my central hypothesis is that, all else equal, Zyprexa's own marketing expenditures will increase quantities sold while competitors' marketing expenditures will decrease quantities sold of Zyprexa.¹⁹⁶

(86) An important weakness of aggregate models such as those adopted here by Professor Rosenthal is that in using only variation over time in promotion and prescribing, estimation of manufacturer-specific detailing effects is challenging, if not impossible. In statistical terms, the model has too few degrees of freedom. It is preferable to start with a disaggregated model that exploits variation over time as well as across geography and/or products to test the assumption that manufacturers' promotional efforts have identical effects. Professor Rosenthal fails to use the available disaggregated data on detailing and prescribing, such as by geography, manufacturer, product, and prescriber, to validate her assumptions. The literature also suggests that aggregate models yield different results from those that examine manufacturers separately. One study of pharmaceutical marketing concludes "the parameter estimates of the individual brand-level models are so different that pooling across brands, even within the same category, is inappropriate."¹⁹⁷

IV.B. The expansion in opioid prescribing is not explained by prescribing of Allergan's products

(87) The scale and timing of Allergan product prescribing is inconsistent with Allergan promotion having contributed to an increase in overall opioid prescribing. The bars in Figure 12–Figure 14 show opioid MMEs dispensed annually from 1997–2017, segmented between Kadian and Norco and all other opioid products. I include separate figures for Cuyahoga and Summit counties and for the entire United States. In both these two counties and nationally, MMEs increase steadily from 1997 through 2010, peak in 2011, and decline thereafter. MMEs associated with Allergan products, shown in yellow for Kadian and blue for Norco at the bottom of the figures, are barely visible.

¹⁹⁶ Exhibit E, Declaration of Meredith Rosenthal, *Hood v. Eli Lilly & Co*, No. 1:07-cv-00645-JBW-RLM, Dkt. 208-4, at 4772 (E.D.N.Y Oct. 9, 2009) ¶ 36–38.

¹⁹⁷ Peter S. H. Lieflang and Jaap E. Wieringa, "Modeling the Effects of Pharmaceutical Marketing," *Marketing Letters* 21, no. 2 (2010), 131.